

cont.

wherein R₁ is lower alkyl, R₂, R₃, R₄ and R₅ are individually selected from the group consisting of hydrogen, halogen and -OSO₂R₁₀, R₆ is -(CH₂)_m-SiR₇R₈R₉, R₇, R₈ and R₉ are individually lower alkyl, R₁₀ is lower alkyl unsubstituted or substituted with at least one halogen or aryl unsubstituted or substituted with at least one lower alkyl, m is an integer from 0 to 6 and its non-toxic, pharmaceutically acceptable salts.

C2

Claim 26 (amended) An antitumoral composition comprising an antitumorally effective amount of a compound of formula (II_A) of claim 24.

PLEASE ADD THE FOLLOWING CLAIM:

C3

--27. A method of treating tumors in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antitumorally effective amount of a compound of claim 24.

REMARKS

Reconsideration of this application is requested in view of the amendments to the claims and the remarks presented herein.

The claims remaining in the application are claims 5, 24, 26 and 27, all other claims having been cancelled. Applicants reserve the right to file divisional applications to the non-elected

inventions.

Claim 26 was rejected under 35 USC 112, second paragraph, as being indefinite and the claims have now been modified to be drawn to a pharmaceutical composition to comply with the U.S. practice. Therefore, withdrawal of this ground of rejection is requested.

Claims 4, 5, 24 and 26 were rejected under 35 USC 102 as being anticipated by the Curran et al patent which, according to the Examiner, discloses compounds of the invention wherein R₅ is alkyl, R₆ is a silicon-containing compound and R₁ to R₄ are hydrogen, halogen or other group and refers to the compounds in lines 35 to 50 of column 13.

Applicants respectfully traverse this ground of rejection since the Curran et al patent is not a proper reference for the above application. The Curran et al patent has a U.S. filing date of April 9, 1999, while the present application is entitled to the French priority date of February 26, 1999. The present disclosure corresponds to that in the French priority application and fully supports the present claims. Therefore, withdrawal of this ground of rejection is requested.

Claims 4, 25 and 26 were rejected under 35 USC 102 as being anticipated by the Biggs et al U.S. Patent and Biggs et al '876 patent which corresponds to the U.S. Patent. The said claims were

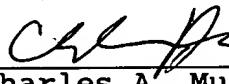
also rejected as being obvious over the '876 reference.

Applicants respectively traverse these grounds of rejection since the Biggs et al references do not disclose silyl substituted compounds in R₆ position. This group increases the lipophilicity of the compounds to present a different tissular distribution. Withdrawal of these grounds of rejection are therefore requested.

It should be noted that Applicants have submitted new claim 27 which is drawn to the method of use of the compounds of claim 24.

In view of the above remarks and the amendments to the claims, it is believed that the claims clearly point out Applicants patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
BIERMAN, MUSERLIAN AND LUCAS

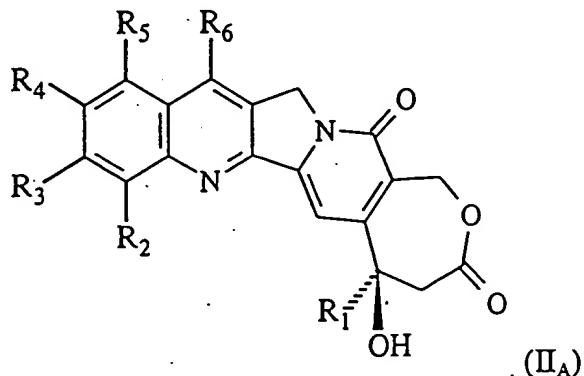

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~~and its non-toxic, pharmaceutically acceptable salts.~~

24. A compound selected from the group consisting of the formula



wherein R₁ is lower alkyl, R₂, R₃, R₄ and R₅ are individually selected from the group consisting of hydrogen, halogen and -OSO₂R₁₀, R₆ is selected from the group consisting of hydrogen, alkyl of 1 to 12 carbon atoms unsubstituted or substituted with at least one halogen, hydroxy lower alkyl, lower alkoxy lower alkyl, cycloalkyl, cycloalkyl lower alkyl, -NO₂, halogen, -(CH₂)_m-SiR₇R₈R₉ and aryl and aralkyl, both unsubstituted or substituted on the aryl with at least one member of the group consisting of lower alkyl, -OH, -CF₃, -OCF₃, -NH₂, halogen, lower alkylamino and dilower alkylamino; R₇, R₈ and R₉ are individually lower alkyl, R₁₀ is lower alkyl unsubstituted or substituted with at least one halogen or aryl unsubstituted or substituted with at least one lower alkyl and m is an integer from 0 to 6 with at least one of R₇, R₈, R₉ and R₁₀ being -OSO₂R₁₀ and/or R₂ is halogen and/or R₃ is selected from the group

consisting of alkyl of 7 to 12 carbon atoms, $(CH_2)_n-SiR_1R_2R_3$, and aryl substituted with at least one member of the group consisting of $-OEt$, and dilower alkylamino and its non-toxic, pharmaceutically acceptable salts.

25. A compound of claim 23 wherein R₁ is ethyl.

PLEASE AMEND THE FOLLOWING CLAIMS:

4. (twice amended) A compound of claim 24 selected from the group consisting of:

(5*R*)-5-ethyl-8-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine 3,15-dione;

(5*R*)-5-ethyl-9,10-difluoro-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-5-ethyl-5-hydroxy-12-(2-trimethylsilylethyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-12-decyl-5-ethyl-9-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-12-decyl-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-12-decyl-5-ethyl-9,11-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-5-ethyl-9-fluoro-5-hydroxy-12-(4-trifluoromethoxyphenyl)-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-12-(4-dimethylaminophenyl)-5-ethyl-9-fluoro-5-hydroxy-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinoleine-3,15-dione;

(5*R*)-5-ethyl-9-fluoro-5-hydroxy-3,15-dioxo-4,5,13,15-tetrahydro-1*H*,3*H*-oxepino [3',4':6,7]indolizino[1,2-*b*]quinolein-10-yl trifluoromethanesulfonate.

22. (amended) A method of treating parasitic infections in warm-blooded animals comprising administering to warm-blooded animals in need thereof an antiparasitically effective amount of a compound of claim 23.

ADD THE FOLLOWING CLAIM:

An antifungal composition comprising an antifunally effective amount of
--26. *As medicament, a compound of formula (II_A) of claim 24 or*
a therapeutical salt thereof.--

REMARKS

The amendment is presented to amend the compound claims to conform to the American practice. PTO Form 2038 for \$80.00 is submitted for the additional claim.

Respectfully submitted,
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PTO Form 2038